



UNITED STATES  
PATENT AND  
TRADEMARK OFFICE

UNDER SECRETARY OF COMMERCE FOR INTELLECTUAL PROPERTY AND  
DIRECTOR OF THE UNITED STATES PATENT AND TRADEMARK OFFICE  
WASHINGTON, D.C. 20231  
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APR 19 2002

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In re Application :  
Milbrandt et al :  
Serial No. 09/473,551 :DECISION ON PETITION  
Filed: 28 December 1999 :  
Attorney Case No. 6029-9879 :

This is in response to applicants' Petition filed 26 December 2001, for review under 37 CFR 1.144 of the restriction requirement set forth on 29 May 2001 as Paper No 10. The delay in acting upon this petition is regretted.

#### BACKGROUND

A review of the file shows that this application was filed under 35 USC 111(a) on 28 December 1999.

In Paper No. 10, the examiner set forth under 35 USC 121 a twenty-way restriction requirement between products and methods. The restriction between the methods and products is not being petitioned and is not further discussed in this Decision. In Paper No. 10, the examiner also set forth a restriction between the growth factors SEQ ID NO: 1-28 recited within each Group, which is under traverse.

The relevant section of the restriction requirement stated that

*The claims of Groups I-XX are drawn to a multitude of growth factors (SEQ ID NO: 1-28), polynucleotides encoding such, and methods of using the growth factor/polynucleotide encoding/cell containing the polynucleotide encoding. This constitutes recitation of an implied, mis-joined Markush group that contains multiple independent and distinct inventions. Each of the different growth factors/nucleic acids and*

*methods of use are independent and distinct because no common structural or functional properties are shared. Burden is established because each growth factor has a unique sequence and therefore, requires a separate search, as it the same for the encoding polynucleotide and methods of use. Accordingly, these claims are subject to restriction under 35 USC 121.*

*“upon election of one of Groups I-XX, Applicants is additionally required to elect a single growth factor or polynucleotide (i.e., a single molecular embodiment which may be represented by a sequence identifier). This requirement is not to be construed as a requirement for an election of species, since each of the compounds recited in the alternative form is not a member of a single genus of invention.”*

In Paper No. 11, filed 2 August 2001, Applicants elected Group I, Groups 1-9, drawn to growth factor comprising human persephin (SEQ ID NO 1, with the F2c and F2a regions comprising human GDNF F2c and F2a, respectively, (SEQ ID NO: 20 and 17). The elected chimeric peptide comprises SEQ ID No 23 and consists of SEQ ID No 26. The election was made with traverse. Claims 1-36 were canceled.

The traversal was on the grounds that human, mouse and rat persephin (SEQ ID No: 1-3) are a reasonable number of species within the genus of persephin. Applicants point out that the invention is not claiming persephin and all chemical combinations thereof, but merely claim a persephin that contains specific combinations of eleven to twelve amino acid substitutions that span a very narrow portion of the molecule namely the F2a and F2c regions, wherein each set of substitutions confer GFR(alpha)1 specificity.

In Paper No. 10, mailed 13 September 2001, the examiner considered the traversal and found the argument that that SEQ ID NO: 1-3 are a number of species within the genus of persephin non-persuasive. The Examiner reasoned that because the different forms of persephin (human, rat and mouse) represent chemically, structurally and functionally different compounds, which can be made and used without each other, they represent patentably distinct inventions itself. The examiner concluded that the claimed different persephin molecular embodiments containing specific amino acid substitutions constitute independent and patentably distinct inventions, since they all have different chemical structures, different functions and can be made and used without each other (see MPEP 806.04, 808.01). The restriction requirement was made Final.

Applicants submitted this Petition, filed as Paper No. 19 on 17 December 2001. The Petition requests review of the requirement for restriction to a single molecular embodiment of a growth factor in the instant application. A declaration from Dr. Milbrandt was attached as Exhibit A and a sequence alignment of the specific growth factor molecular embodiments under dispute was attached as Exhibit B. Applicants traverse the “single molecular embodiment” restriction. Applicants consider that this restriction is most appropriately a species election and not an election restriction. The Petition presented new arguments and evidence, including the declaration and sequence alignments. Applicants argued that the human, mouse and rat sequences presented in the

instant application are obvious embodiments of the same growth factor and are thus not patentably distinct.

The Declaration of Dr. Milbrandt states that one of ordinary skill in the art would consider closely related mammalian homologs of the same growth factor to be essentially and effectively the same growth factor or at the very least, species within a genus. (Paragraph 6). The Declaration states that the persephins with SEQ ID NO: 1-3 are virtually identical in amino acid sequence and have indistinguishable growth factor properties and biological activity. The Declaration and the sequence alignments show the percentages of identity, similarity or conservative residues. The Declaration discussed the way other applications have been treated by the Office with regards to restriction requirements.

## DISCUSSION

The Petition and its exhibits, Declaration of Dr. Milbrandt and sequence alignments have been considered carefully. The claims, the restriction requirement and the Petition, will be discussed each in turn.

Original Claim 1 recited:

A growth factor which activates GRF(alpha)1-RET but does not substantially activate GFR(alpha)2-Ret or GFR(alpha)3-Ret.

No structural limitations or single molecular embodiments were provided in original claim 1. Dependent claim 3 set forth some structural constraints, that 1-8 residues of the F2a region are identical to GDNF or conservative amino acid substitutions, therefore and that 1-8 residues of the F2c region are identical to GDNF or conservative amino acid substitutions, therefore. Claim 4 recites additional structural limitations for portions of the claimed persephins. The elected single molecular embodiments (SEQ ID NO: 23 and 26) are presented in dependent claims 7 and 8.

When claims link distinct inventions, MPEP 809 states that a restriction can nevertheless be required. MPEP 809.03 provides guidance for the treatment of linking claims.

Claims 1 and 6 link the inventions of claim 7 (SEQ ID No 23) and claim 8 (SEQ ID NO 26). The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s). Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C.

121 are no longer applicable. In re Ziegler, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

The restriction requirement between the various sequences, while essentially correct, was set forth between chimeric persephins of SEQ ID NO: 1-28. Upon further review, it is noted that SEQ ID NO: 1-22 only define portions of growth factors, which are used, in whole or in part to build the various chimeric growth factors. SEQ ID NO: 23-28 define the single molecular embodiments of full-length chimeric growth factors. The single molecular embodiments are presented in dependent claims 7 and 8 and not in Claims 1 and 6. Linking claims 1 and 6 and their treatment during examination, appear to have been overlooked in the restriction requirement. Since the original restriction requirement was directed to the single molecular embodiments, a selection between SEQ ID NO: 23-28 should have been set forth. Applicants elected human persephin (SEQ ID NO 1 comprising GDNF F2c and F2a (SEQ ID NO: 20 and SEQ ID NO 17), which correspond to a peptide that comprises SEQ ID NO 23 and consists of SEQ ID NO: 26. Thus the Office has provided an examination of two single molecular embodiments and of the linking claims.

Applicants' arguments are primarily directed to the single molecular embodiments and not to the full scope of the claims. Exhibit B shows an amino acid alignment of between human, mouse and rat persephins (SEQ ID NO: 1, 2 and 3, respectively). Exhibit B does not provide an alignment comparing the chimeric growth factor products SEQ ID NO: 23-28.

Applicants' statement that the human, mouse and rat sequences are obvious embodiments of the same growth factor and are thus not patentably distinct is noted. Again, the statement of obviousness is not directed to the claimed chimeric growth factors (SEQ ID NO: 23-28) but to the building blocks from which the chimeric proteins are produced. . These statements and sequence alignment are not commensurate in scope with the claimed subject matter. None of the claims are directed to or encompass the human, mouse or rat persephin with SEQ ID NO: 1, 2 or 3. The claims are drawn to chimeric growth factors in which the human, mouse or rat persephin is altered to include a GDNF sequences in place of persephin sequences in domains F2a and F2c.

Should applicant traverse on the ground that the chimeric persephins of SEQ ID NO: 23-28 are not patentably distinct, applicant should submit or provide such evidence or identify such evidence now of record showing the sequences to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 USC 103(a) of the other invention.

In Paper No. 21, the Examiner examined amended claims 1 and 6-9 in so far as they are drawn to the elected invention, chimeric peptides of SEQ ID No 23 and SEQ ID No; 26. The rejection under 35 USC 112, first paragraph, of Claims 1 and 6-9 was maintained for lack of enablement. Should claims 1 and 6 linking the elected chimeric persephins of

SEQ ID NO: 23 and 26 become allowable, MPEP 809.04 provides direction for the treatment of claims directed to the other sequences.

## DECISION

Applicants' petition is **DENIED** for the reasons set forth above.

Applicants remain under obligation to properly respond to the Final Office Action mailed 22 January 2002, within the time period set therein or as extendable under the provisions of 37 CFR 1.136(a).

Any request for reconsideration of this decision must be made by way of a renewed petition and must be filed within TWO MONTHS of the date of mailing of this decision in order to be considered timely.

Should there be any questions with respect to this decision, please contact Special Program Examiner Julie Burke by letter addressed to the Director, Technology Center 1600, Washington DC 20231. Alternatively, SPRE Burke can be reached by telephone at (703) 308-7553 or by facsimile transmission at (703) 305-7230.

A handwritten signature in black ink, appearing to read 'Bruce M. Kisliuk', written in a cursive style.

Bruce M. Kisliuk  
Director, Technology Center 1600